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(FILE 'HOME' ENTERED AT 10:04:03 ON 29 AUG 2003)

FILE 'USPATFULL' ENTERED AT 10:04:12 ON 29 AUG 2003

L1	2 S 112676-85-4/RN
L2	0 S 11267666-86-5/RN
L3	2 S 112676-86-5/RN
L4	2 S L1 OR L3
L5	2 S L4 AND (BENZAMIDE)
L6	2 S L4 AND ((BENZAMIDE) (P) PYRIMIDINYL)
L7	2 S L4 AND ((BENZAMIDE) (P) PYRIMIDINYL (P) PRIDINYL)
L8	2 S L7 AND (BENZAMIDE (P) METHYL (P) PYRIDINYL (P) PYRIMIDINYL (P
L9	0 S L7 AND (BENZAMIDE (W) METHYL (W) PYRIDINYL (W) PYRIMIDINYL (W

L4 ANSWER 3 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1998:137625 CAPLUS
 DN 128:281507
 TI Microvascular endothelial activation in the skeletal muscles of patients with multiple organ failure
 AU Helliwell, Timothy R.; Wilkinson, Ann; Griffiths, Richard D.; Palmer, T. E. Alan; McClelland, Peter; Bone, J. Michael
 CS Daulby Street, Duncan Building, Department of Pathology, University of Liverpool, Liverpool, L69 3GA, UK
 SO Journal of the Neurological Sciences (1998), 154(1), 26-34
 CODEN: JNSCAG; ISSN: 0022-510X
 PB Elsevier Science B.V.
 DT Journal
 LA English
 CC 14-15 (Mammalian Pathological Biochemistry)
 AB The relationship between microvascular damage and the presence of muscle fiber atrophy and necrosis has been investigated in skeletal muscle biopsies taken from 57 patients with multiple organ failure. Immunohistochem. studies showed no loss of capillaries and no luminal thrombosis, while neutrophil leukocytes were more prevalent in the patients' biopsies than in controls. Deposition of the complement membrane attack complex (C5-9MAC) in capillaries was obsd. in 41 of cases. Endothelial activation was suggested by an increased intensity of expression of ICAM-1, and by an increased proportion of capillaries expressing P selectin and E selectin, although this was not directly assocd. with neutrophil accumulation. Endothelial swelling was present in many biopsies with 38 of the biopsies having larger capillary profiles on immunohistochem. labeling for von Willebrand factor (vWF), thrombomodulin and CD34, and on Ulex europaeus agglutinin 1 binding. Endothelial swelling was confirmed by image anal. and morphometric evaluation of capillary ultrastructure, however, the capillary luminal area was not reduced as the capillaries were dilated. Increased vWF labeling was assocd. with C5-9MAC deposition and with fiber necrosis, but the vascular changes were not related to fiber atrophy nor to clin. indexes of the severity of the patients' illness. The results suggest that microvascular damage and ischemia may not be major factors in the pathogenesis of muscle fiber damage in multiple organ failure, but that endothelial activation is a common occurrence. The variability in the patterns of markers of endothelial activation, and the small proportion of capillaries affected, may reflect the complexity of the endothelial response to circulating or locally produced cytokines.
 ST multiple organ failure muscle atrophy biochem
 IT Selectins
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (E-; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
 IT Cell adhesion molecules
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (ICAM-1 (intercellular adhesion mol. 1); microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
 IT Selectins
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (P-; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
 IT Muscle, disease
 (atrophy; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
 IT Blood vessel, disease
 (endothelium, injury; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)

IT Multiple organ failure
Multiple organ failure
(microvascular endothelial activation in skeletal muscles of humans
with multiple organ failure)

IT CD34 (antigen)
Thrombomodulin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(microvascular endothelial activation in skeletal muscles of humans
with multiple organ failure)

IT Blood vessel
Blood vessel
(microvessel, endothelium; microvascular endothelial activation in
skeletal muscles of humans with multiple organ failure)

IT Muscle, disease
Muscle, disease
(necrosis; microvascular endothelial activation in skeletal muscles of
humans with multiple organ failure)

IT 82986-89-8, Complement C5b9 109319-16-6
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(microvascular endothelial activation in skeletal muscles of humans
with multiple organ failure)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L4 ANSWER 11 OF 46 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 1999423977 EMBASE
 TI [Pathophysiology and diagnosis of coagulation activation in sepsis].
 PATHOPHYSIOLOGIE UND DIAGNOSTIK DER GERINNUNGSAKTIVIERUNG BEI SEPSIS.
 AU Ostermann H.; Bohrer H.
 CS Dr. H. Ostermann, Medizinische Klinik/Poliklinik III, Ludwig-Maximilians-
 Univ. Munchen, Marchioninistrasse 15, D-81377 Munchen, Germany
 SO Anesthesiologie und Intensivmedizin, (1999) 40/11 (796-799).
 Refs: 32
 ISSN: 0170-5334 CODEN: ANIMD2
 CY Germany
 DT Journal; Article
 FS 024 Anesthesiology
 025 Hematology
 LA German
 SL English; German
 AB Sepsis can be regarded as a systemic inflammatory reaction often
 accompanied by disseminated intravascular coagulation (DIC) which is
 supposed to be initiated by the expression of tissue factor for example by
 activated monocytes and endothelial cells. The hallmark of DIC is the
 intravascular generation of thrombin which leads to fibrin formation.
 Diagnosis of DIC is likely if sepsis is accompanied by the occurrence of
 intravascular soluble fibrin, a decrease in coagulation inhibitors
 (antithrombin) and thrombocytopenia. The most sensitive and specific test
 for DIC seems to be the detection of fibrin monomers. Clinical symptoms of
 DIC are caused simultaneously by consumption of coagulation factors
 (bleeding) and intravascular **thrombosis (organ**
failure).
 CT Medical Descriptors:
 *sepsis
 *disseminated intravascular clotting
 blood clotting
 monocyte
 endothelium cell
 fibrin formation
 disease association
 human
 article

L4 ANSWER 12 OF 46 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 1999362498 EMBASE
 TI Coagulation and fibrinolysis in patients undergoing operation for ruptured and nonruptured infrarenal abdominal aortic aneurysms.
 AU Adam D.J.; Ludlam C.A.; Ruckley C.V.; Bradbury A.W.
 CS D.J. Adam, Vascular Surgery Unit, Univ. Dept. of Clinic./Surg. Sci., Royal Infirmary, Edinburgh EH3 9YW, United Kingdom
 SO Journal of Vascular Surgery, (1999) 30/4 (641-650).
 Refs: 31
 ISSN: 0741-5214 CODEN: JVSUES
 CY United States
 DT Journal; Article
 FS 009 Surgery
 018 Cardiovascular Diseases and Cardiovascular Surgery
 037 Drug Literature Index
 LA English
 SL English
 AB Purpose: Hemorrhage and **thrombosis** predisposing to myocardial infarction, multiple **organ failure**, and thromboembolism account for the majority of the morbidity and mortality associated with repair of ruptured and nonruptured abdominal aortic aneurysms (AAAs). The aim of this study was to examine coagulation and fibrinolysis in patients operated on for ruptured and nonruptured infrarenal AAAs. Methods. Ten patients operated on for ruptured and 9 patients operated on for nonruptured AAAs were studied. Tissue plasminogen activator (t-PA) antigen, thrombinantithrombin (TAT), and D-dimer were measured before induction of anesthesia. Plasminogen activator inhibitor (PAI) activity, t-PA activity, and prothrombin fragment (PF) 1+2 were measured before induction of anesthesia, immediately before aortic clamp release, and 5 minutes and 24 hours after aortic clamp release. Results: Preoperatively, ruptured AAA was associated with significantly elevated t-PA antigen (median 15.7 ng/mL, range 9.0 to 22.1 ng/mL versus nonrupture: median 6.6 ng/mL, range 4.7 to 16.4 ng/mL; $P < .01$, Mann-Whitney test), increased PAI activity (median 36.5 arbitrary units/mL, range 20.6 to 38.8 arbitrary units/mL versus nonrupture: median 8.2 arbitrary units/mL, range 3.2 to 21.7 arbitrary units/mL; $P < .001$), reduced t-PA activity (median 0.12 IU/mL, range 0.06 to 0.4 IU/mL versus nonrupture: median 0.49 IU/mL, range 0.14 to 3.2 IU/mL; $P < .01$), elevated TAT (median 135.5 $\mu\text{g/L}$, range 61.2 to 209.4 $\mu\text{g/L}$ versus nonrupture: median 21.6 $\mu\text{g/L}$, range 6.6 to 180.4 $\mu\text{g/L}$; $P < .02$) and elevated PF 1+2 (median 9.0 nmol/L, range 5.4 to 11.6 nmol/L versus nonrupture: median 2.2 nmol/L, range 0.7 to 7.1 nmol/L, $P < .001$). There was no significant difference in preoperative D-dimer levels (median 3460 ng/mL, range 1236 to 7860 ng/mL versus nonrupture: median 1642 ng/mL, range 728 to 5334 ng/mL; $P = .07$). The differences in PAI activity, t-PA activity, and PF 1+2 persisted throughout the course of surgery, but there was no significant difference between the groups at 24 hours. Conclusion: These novel data demonstrate that ruptured AAA repair is associated with inhibition of systemic fibrinolysis and intense thrombin generation. Similar changes are seen in nonruptured AAA but are of a lesser magnitude. This procoagulant state may contribute to the microvascular and macrovascular **thrombosis** that leads to myocardial infarction, multiple **organ failure**, and thromboembolism.
 CT Medical Descriptors:
 *abdominal aorta aneurysm: SU, surgery
 *aneurysm rupture: SU, surgery
 *thromboembolism: CO, complication
 *thromboembolism: DT, drug therapy
 *thromboembolism: PC, prevention
 *heart infarction: CO, complication
 *heart infarction: DT, drug therapy
 *heart infarction: PC, prevention
 multiple organ failure: CO, complication

multiple organ failure: DT, drug therapy
multiple organ failure: PC, prevention
aneurysm surgery
thrombosis prevention
anticoagulant therapy
heparinization

human

male

female

clinical article

aged

article

priority journal

Drug Descriptors:

*heparin: DT, drug therapy

tissue plasminogen activator

RN (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (tissue plasminogen
activator) 105913-11-9

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L1 1 WO2001012621/PN
(WO2001012621/PN)

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L1 ANSWER 1 OF 1 INPADOC COPYRIGHT 2003 EPO on STN

PATENT FAMILY INFORMATION
AN 145684263 INPADOC

+-----PRAI-----+
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4 priorities, 10 applications, 11 publications

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